Complete Summary

GUIDELINE TITLE

Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 25 p. (Technology appraisal guidance; no. 139).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Obstructive sleep apnea/hypopnea syndrome

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Pulmonary Medicine
Sleep Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnea/hypopnea syndrome (OSAHS)

TARGET POPULATION

Adults with symptomatic obstructive sleep apnea/hypopnea syndrome (OSAHS)

INTERVENTIONS AND PRACTICES CONSIDERED

Continuous positive airway pressure (CPAP)

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Subjective sleepiness as assessed by the Epworth Sleepiness Scale (ESS)
    - Objective sleepiness as assessed by Maintenance of Wakefulness Test (MWT), Osler test, Multiple Sleep Latency Test (MSLT), or equivalent measure
    - Blood pressure
    - Cardiovascular disease
    - Accidents (e.g., driving, occupational)
    - Quality of life
    - Mood, anxiety, and depression
    - Simulated driving performance
    - Neuropsychological functioning
    - Apnea/hypopnea index (AHI)/desaturation rate
    - Any complications or adverse effects of treatment
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York. (See the "Availability of Companion Documents" field).

Clinical Effectiveness

Search Strategy

The search terms used to capture the concepts of sleep apnoea and continuous positive airway pressure (CPAP) were arrived at by discussion with reviewers and experts. These search terms were then adapted for each individual database and relevant thesaurus terms used where possible. The search strategies used for each database are included in Appendix 11.1 of the Assessment Report (see the "Availability of Companion Documents" field).

A range of databases and websites were searched to identify existing systematic reviews and guidelines on CPAP for sleep apnoea:

- Cochrane Database of Systematic Reviews (Cochrane Library 2006, issue 3) (www.thecochranelibrary.com)
- Database of Abstracts of Reviews of Effects (CRD's administration version of the database)
- Health Technology Assessment Database (CRD administration version of the database)
- Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk)
- National Guideline Clearinghouse (http://www.guideline.gov/)
- National Research Register (2006, issue 3) (http://www.update-software.com/National/)
- Health Services/Technology Assessment Text (HSTAT) (http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat)
- Turning Research into Practice Database (Trip) (http://www.tripdatabase.com/)
- Health Evidence Bulletins Wales (http://hebw.cf.ac.uk/index.html)
- Clinical Evidence (http://www.clinicalevidence.com)
- National Library for Health Guidelines Finder (http://www.library.nhs.uk/guidelinesfinder/)

Further databases were searched to identify primary studies:

- MEDLINE (1966-November week 3 2006) (OVID)

- MEDLINE In-Process & Other Non-Indexed Citations (November 28 2006) (OVID)
- EMBASE (1980-2006 week 47) (OVID)
- Cochrane Central Register of Controlled Trials (Cochrane Library 2006, issue 4) (www.thecochranelibrary.com)
- CINAHL (1982-November week 3 2006) (OVID)
- Science Citation Index (1900-November 25 2006) (Web of Knowledge)
- ISI Proceedings Science & Technology (1990-November 25 2006) (Web of Knowledge)
- Zetoc Conferences (1993-November 29 2006) (http://zetoc.mimas.ac.uk/)

The contents pages of nine journals (selected by the review team based on included references from a previous systematic review on this topic) were also hand searched to identify reports which might not have been indexed by the electronic databases. In addition, electronic alerts were set up for each journal so that the contents page could be scanned as the latest edition was published.

A selection of conference proceedings based on recommendations from the Cochrane Airways Group were also scanned for relevant abstracts.

See Section 5.1.1 of the Assessment Report (see the "Availability of Companion Documents" field) for information on journal titles and conference names.

The industry submissions were also searched for any additional unpublished data. No additional studies were identified.

Inclusion and Exclusion Criteria

Titles and abstracts identified from the searches were independently screened for relevance by two reviewers and disagreements were resolved by consensus. The full papers were ordered for all potentially relevant studies. Full papers were screened independently by two reviewers based on the inclusion criteria below. Disagreements were resolved by consensus and, if necessary, a third reviewer was consulted. Studies in any language were included in the review if they meet the following criteria.

Population

Studies of adults (16 years or older) with a diagnosis of predominantly obstructive sleep apnoea, confirmed by use of an appropriate tool (for example, a respiratory polysomnographic sleep study, analysed by an appropriately qualified respiratory physician, from which a standard severity criteria such as the apnoea/hypopnoea or arterial oxygen desaturation index has been derived) were included. Populations of any disease severity were eligible. Studies of participants with central nervous system (CNS) dysfunction (e.g., stroke or dementia such as Alzheimer's disease) and heart failure were excluded. However, studies of general population groups that may have had some patients with these co-morbid conditions were included.

Intervention and Comparators

Studies of fixed CPAP or autotitrating CPAP therapy were eligible for inclusion provided the treatment was of at least one week duration. For the purposes of this review fixed and autotitrating CPAP were treated as the same intervention: studies comparing the two technologies were not eligible for inclusion. Relevant comparators were best supportive/usual care (including conservative intervention such as lifestyle advice regarding weight loss, alcohol consumption and sleep hygiene as well as sleep posture advice or treatment), placebo (including placebo pill and sham CPAP) and dental devices. For sham CPAP the sub-therapeutic pressure used varies between studies. The Assessment group included studies where it was stated sham CPAP and did not exclude studies based on the specific the sub-therapeutic pressure used.

Outcomes

The following outcomes were included:

Primary Outcomes

- Subjective sleepiness as assessed by the Epworth Sleepiness Scale (ESS)
- Objective sleepiness as assessed by Maintenance of Wakefulness Test (MWT), Osler test, Multiple Sleep Latency Test (MSLT), or equivalent measure

Secondary Outcomes

- Blood pressure (mean day and night blood pressure were assessed separately as the mechanisms and patterns of daytime and nighttime blood pressure disturbance in obstructive sleep apnoea/hypopnoea syndrome (OSAHS) vary, and the relationship between daytime blood pressure and vascular risk has been more clearly described in other studies)
- Cardiovascular disease (e.g., myocardial infarction, stroke)
- Accidents (e.g., driving, occupational), though it was thought unlikely that such data would be found in randomised controlled trials (RCTs)
- Quality of life, where it was measured using a standardised scale
- Mood, anxiety and depression, where it was measured using a standardised scale
- Simulated driving performance
- Neuropsychological functioning
- Apnoea/hypopnoea index (AHI)/desaturation rate
- Any complications or adverse effects of treatment

Outcomes such as changes to sleep architecture (e.g., rapid eye movement sleep, slow-wave sleep, sleep efficiency) were not considered.

Study Design

Randomised controlled trials using a parallel or crossover design were included. In this field there is no standard practice as to whether a washout period is used in crossover trials and, if so, how long the washout period should be. Because the effect of CPAP in relation to daytime sleepiness is thought to be short-lived, the risk of carryover was not considered to be a serious problem.

Cost-Effectiveness

Papers obtained from the clinical effectiveness review were scanned to check whether they included cost-effectiveness data. In addition, several economic databases were searched for cost-effectiveness studies as listed below (for full details refer to Appendix 11.1.3 of the Assessment Report [see the "Availability of Companion Documents" field]).

- MEDLINE and in process MEDLINE and other non-indexed citations (1950- Jan 10 2007) (OVID)
- EMBASE (1980-2007 week 1) (OVID)
- Cochrane Central Register of Controlled Trials (Cochrane Library 2006, issue 4) (www.thecochranelibrary.com)
- NHS Economic Evaluation Database (NHS EED) (CRD internal administration system 13/1/07)
- Health Economic Evaluations Database (HEED) (1995-Jan 2007) (CD-ROM)
- HTA database (CRD internal administration system 13/1/07)
- EconLit (1969-2006/10) (SilverPlatter)
- EconPapers (http://econpapers.repec.org/)

A broad range of studies was considered in the assessment of cost-effectiveness, including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Studies were included in the cost-effectiveness review if they considered the costs and outcomes associated with two or more interventions in the treatment of OSAHS. Therefore, studies based on cost-consequence analysis, cost-utility analysis, cost-effectiveness analysis, cost-minimisation analysis, and cost-benefit analysis were eligible for inclusion.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Forty-eight studies (101 papers: 55 full papers and 46 abstracts/conference proceedings)

Cost-Effectiveness

- Four published economic evaluations
- One manufacturer submission

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York. (See the "Availability of Companion Documents" field).

Clinical Effectiveness

Data Extraction

The authors of a recent systematic review provided the extracted data from their review to avoid duplication of work. This also included some unpublished data. These data had been independently extracted by two reviewers. Data from the new studies, as well as any additional data required from the studies previously extracted were extracted by one reviewer and checked by another. Discrepancies were resolved by discussion and, if necessary, a third reviewer was consulted. Where there were multiple publications from the same study, the main publication for each study was identified and data were extracted from that paper. Where additional relevant outcomes were available in a related paper these were also extracted.

Data were extracted into Revman and into a standard form in Word. Data extracted included patient characteristics (age, sex, severity of obstructive sleep apnoea/hypopnoea syndrome [OSAHS], body mass index), details of the intervention (fixed or autotitrating continuous positive airway pressure [CPAP], use of humidifier), comparator (details of placebo, conservative management or dental device), adherence (usually reported as the average number of hours the machine was running at night), length of follow-up, outcomes and study quality.

Predominantly endpoint data were reported in the trials, except for blood pressure where a mixture of change and endpoint data were reported. Where both endpoint and change data were reported, preference was given to endpoint data for all outcomes except blood pressure where change data were used (provided the variance for the change score was reported). Where only change data were reported, the variance was imputed if necessary.

Paired data were extracted from crossover trials where available. If the standard deviation (SD) or standard error (SE) from a paired analysis was not reported, the standard error was imputed from the *t*-statistic, the *p*-value or the confidence interval from a paired analysis. For one crossover study it was necessary to impute the standard error for blood pressure: a within-person correlation of 0.5 was used and a within-person correlation of 0.1 and 0.9 for a sensitivity analysis.

Due to time limitations and the quantity of cognitive data from crossover trials it was not feasible to impute data for a paired analysis, where these were not reported, for all the cognitive outcomes. Where three or more studies were available for potential pooling, the SE was estimated where data were available as above. For the other cognitive outcome measures the mean end value at follow-up and the SD for the intervention and control group with the associated *p*-value were extracted. Where available the SD or SE from a paired analysis were extracted.

Quality Assessment

Study quality was assessed based on criteria from CRD Report No 4 and additional criteria were used to assess crossover trials (see Section 5.2.1.2 of the Assessment Report [see the "Availability of Companion Documents" field]). The criteria assessed were broad in anticipation that a narrative synthesis may have been necessary. Quality was assessed by one reviewer and checked by another. Discrepancies were resolved by discussion and, if necessary, a third reviewer was consulted.

Data Analysis

Where sufficient data were available, they were pooled in quantitative syntheses using a random effects model. Studies comparing CPAP to placebo or best supportive/usual care were pooled separately from studies comparing CPAP to dental devices. Where data sets included both study designs, parallel and crossover trials were pooled together. The generic inverse variance method in Revman was used to pool data sets which included both parallel and crossover designs, or only crossover trials. When only parallel trials were being pooled the weighted mean difference method in Revman was used. To transform the parallel data for entry into the generic inverse variance facility the standard error for the mean difference was calculated from the 95% confidence interval (CI). This was calculated using the formula SE = (upper CI- lower CI)/3.92. This method assumes a sample size of at least 30, however, given the number of outcomes and studies included in the review it was not considered feasible in the time available to use the *t*-statistic.

Statistical heterogeneity between trials was assessed using the I^2 statistic. Five sources of potential clinical and methodological heterogeneity were identified *a priori* as being of priority: baseline disease severity, baseline daytime sleepiness, study design, type of placebo, and study quality. The Assessment Group planned to investigate these for the primary outcomes using sub-group analysis, since clinically important variations in the magnitude of treatment effects are likely in different severity groups. The sub-groups specified in advance were as follows.

- Population sub-groups:
    - Baseline disease severity, as classified using the apnoea/hypopnoea index (AHI) or the desaturation rate using the mean baseline score for each study: mild (AHI 5-14/hr or oxygen desaturation rate 5-10/hr), moderate (AHI 15-30/hr or oxygen desaturation rate 10-30/hr) and severe (AHI >30/h or oxygen desaturation rate >30/hr)

    - Baseline symptom severity, as classified using the mean baseline Epworth Sleepiness Scale (ESS) score for each study: mild (0 to 9 points), moderate (10 to 15 points) and severe (16 to 24 points).
- Comparator sub-groups:
    - Sham CPAP, oral placebo, and best supportive care.
- Study design sub-groups:
    - Parallel and crossover.
    - Endpoint data and change from baseline data.

The Assessment Group planned to investigate the influence of study quality on the treatment effect by pooling studies with adequate concealment of allocation separately from those with inadequate or unclear adequacy of concealment. This analysis was limited due to the small number of studies that reported an adequate method of concealing treatment allocation.

The pooling of the primary outcomes and blood pressure were rerun using a fixed effect model to test the impact of the model of analysis used. The robustness of the findings for these outcomes was also investigated by assessing the impact on the treatment effect of removing each study singly.

Refer to Sections 5.1.3 -- 5.1.5 and 5.2 of the Assessment Group Report (see the "Availability of Companion Documents" field) for more information.

Cost-Effectiveness

Cost-Effectiveness Review Methods

Data were extracted using a data extraction form that was developed for use in previous Technology Assessment Reviews. The quality of the cost-effectiveness studies was assessed based on a checklist developed by Drummond et al (2005) and which reflects the criteria for economic evaluation detailed in the methodological guidance developed by NICE http://www.nice.org.uk/. (Refer to Appendix 11.6 of the Assessment Report [see the "Availability of Companion Documents" field] for economic evaluation data extraction table and Table 6.27 of the Assessment Report for economic evaluation quality assessment table).

In an attempt to make full use of all of the available evidence on therapies for the treatment of OSAHS and in order to overcome some of the limitations of the published and manufacturer's cost-effectiveness studies, a new cost-effectiveness model was developed by the Assessment Group.

See Section 6.2 of the Assessment Report (see the "Availability of Companion Documents" field) for information about the York economic model.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Four published economic evaluations were identified by the Assessment Group, all of which compared continuous positive airway pressure (CPAP) with a 'do nothing' alternative. The resulting incremental cost-effectiveness ratios (ICERs) were: (1) US $3354 (approximately 1688 pounds sterling; currency conversions were calculated in August 2007) per quality-adjusted life year (QALY) gained from a third-party payer perspective and US $314 (158 pounds sterling) per QALY gained from a societal perspective; (2) 7861 euro (5348 pounds sterling) per QALY gained over a 5-year time horizon and 4938 euro (3359 pounds sterling) per QALY gained for a lifetime time horizon; (3) 8300 pounds sterling per QALY gained at 1 year and 5200 pounds sterling per QALY gained at 2 years; (4) Can $9809 (4654 pounds sterling) per QALY gained for the high-cost estimate and Can $3523 (1672 pounds sterling) per QALY gained for the low-cost estimate.

Fisher & Paykel Healthcare and Respironics UK did not submit its own cost-effectiveness analyses. The Assessment Group therefore evaluated only the economic model submitted by ResMed (UK).

ResMed (UK) submitted an economic model comparing fixed and auto-titrating CPAP devices with a 'do nothing' alternative. The model included people with severe obstructive sleep apnoea/hypopnoea syndrome (OSAHS) with the following health states: event free, cardiovascular event, stroke, and road traffic accident. People remained in one of the four health states for 1 year before moving to another state. People who had a cardiovascular event or road traffic accident in 1 year could have a stroke, cardiovascular event or road traffic accident in a later year. People who had experienced a stroke were considered unable to drive and therefore could not experience a subsequent road traffic accident, but they could experience a subsequent stroke or cardiovascular event. There was no limit to the total number of events each person could undergo in subsequent years. No complications or symptoms were included, and the model had a 14-year time horizon and was from a UK National Health Service (NHS) perspective. Utility estimates were obtained from a published study reporting EuroQoL-5 dimensions (EQ-5D) data. The results of the ResMed (UK) model showed that both fixed and auto-titrating CPAP devices dominated 'non-treatment' after a minimum of 2 years of treatment (that is, CPAP was associated with more QALYs and lower costs than 'non-treatment').

The Assessment Group provided an economic model comparing CPAP with dental devices and with lifestyle management. The base-case model included people with moderate OSAHS and included the following health states: OSAHS, OSAHS post-coronary heart disease (CHD), OSAHS post-stroke, and death. People remained in one of the health states for 1 year, and could remain in the initial OSAHS state until death or until they experienced a road traffic accident, stroke or CHD event, which could result in disability. The OSAHS post-CHD and OSAHS post-stroke states incorporated the increased mortality and morbidity associated with having these events. People could remain in the post-stroke or post-CHD state until

death. No complications or symptoms were included, and the model had a lifetime time horizon and was from a UK NHS perspective.

Health effects in the model included decreased utility associated with Epworth Sleepiness Scale (ESS) score, cardiovascular events, stroke and road traffic accidents, and effects on mortality associated with cardiovascular events, stroke and road traffic accidents. The Assessment Group developed its own mapping algorithm to transform ESS data into utility scores. For this, the Assessment Group used three sets of individual patient data that measured ESS score and SF-36 and/or EQ-5D profile in the same people. A simple linear regression model was fitted to predict absolute utility scores from absolute ESS scores, controlling for baseline utility and ESS scores. This utility mapping was then applied to data on mean difference in ESS score between CPAP and placebo (23 studies) and between CPAP and dental devices (6 studies).

The base-case ICERs for men were 2000 pounds sterling per QALY gained for dental devices compared with lifestyle management, and 3899 pounds sterling per QALY gained for CPAP compared with dental devices. The ICERs for women were similar. The Assessment Group undertook a series of subgroup analyses based on baseline severity of OSAHS as measured by the ESS. This analysis excluded road traffic accidents and cardiovascular events. The resulting ICERs for CPAP compared with lifestyle management were 20,585 pounds sterling per QALY gained for mild OSAHS, 9391 pounds sterling per QALY gained for moderate OSAHS and 4413 pounds sterling per QALY gained for severe OSAHS. Dental devices were extendedly dominated by CPAP for moderate OSAHS, and there were no data for comparisons of dental devices with CPAP for mild or severe OSAHS.

Only two of the Assessment Group's subgroup and scenario analyses resulted in pronounced changes to the base-case ICERs. When the lifespan of the device was changed from 7 to 5 years and an auto-titrating device plus humidifier was used instead of a fixed-pressure device, the ICER was 16,362 pounds sterling per QALY gained. When cardiovascular events and road traffic accidents were excluded in the analysis for the total population (all severities of OHAHS), the ICER was approximately 8000 pounds sterling per QALY gained.

The Committee reviewed the available evidence on the cost effectiveness of CPAP for the treatment of severe OSAHS, namely the analyses from one of the manufacturers (ResMed [UK]) and from the Assessment Group, and noted that the base-case ICERs in both analyses were below 5000 pounds sterling per QALY gained.

The Committee considered the findings of the subgroup analysis for different severity grades of OSAHS. This subgroup analysis was only available excluding cardiovascular events and road traffic accidents. The Committee noted that the ICERs for moderate and severe OSAHS were below 10,000 pounds sterling per QALY gained, even when road traffic accidents were excluded from the economic modelling. It therefore agreed that, for people with moderate or severe OSAHS, CPAP would be an appropriate use of NHS resources and should be recommended as a treatment option.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Continuous positive airway pressure (CPAP) is recommended as a treatment option for adults with moderate or severe symptomatic obstructive sleep apnoea/hypopnoea syndrome (OSAHS).

CPAP is only recommended as a treatment option for adults with mild OSAHS if:

- They have symptoms that affect their quality of life and ability to go about their daily activities, **and**
- Lifestyle advice and any other relevant treatment options have been unsuccessful or are considered inappropriate.

The diagnosis and treatment of OSAHS, and the monitoring of the response, should be carried out by a specialist service with appropriately trained medical and support staff.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnea/hypopnea syndrome (OSAHS)

POTENTIAL HARMS

- Reasons for not adhering to continuous positive airway pressure (CPAP) treatment include poor mask fit, pressure intolerance and, more commonly, upper airway symptoms such as nasal dryness, nasal bleeding and throat irritation.
- Humidification devices are now commonly used in conjunction with CPAP devices in order to reduce these side effects.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Limitations of the Assessment

Clinical Effectiveness

While there is clear and robust evidence of a benefit with continuous positive airway pressure (CPAP) compared to placebo/usual care in relation to daytime sleepiness, the finding of a variation in the treatment effect with disease severity needs to be interpreted with some caution. The factors of interest investigated (except for one post-hoc analysis) were specified in advance and the number of factors investigated was kept as small as possible. In addition, the findings from the sub-group analyses make clinical sense. However, the sub-group analyses are based on summary data and the comparisons are therefore observational and are not based on randomised comparisons as in a trial or an individual patient data analysis. Therefore, the trend of a treatment effect by disease severity should not be considered definitive. In addition, although the cut-off points used to define disease (apnoea/hypopnoea index [AHI]) and symptom severity (the Epworth Sleepiness Scale [ESS]) are based on those used clinically, these are arbitrary cut-off points. The sub-group analyses for other outcomes were limited by the small number of studies available. However, because disease and symptom severity are thought to be clinically important factors in the response to treatment the Assessment Group has tried to make clear the clinical populations to which the findings refer.

Cost-Effectiveness

The York model provided an estimate of the value of further research, which indicated that the cost of the uncertainty associated with the model parameters was high. The expected value of perfect information (EVPI) was calculated based

only on the incident patient population and does not incorporate uncertainty in model structure, modelling assumptions and data quality. As such it may underestimate the cost of the decision uncertainty. When interpreting the results of the York model some caveats must be borne in mind:

- The translation of health benefits in terms of ESS to utility scores was based on simple regression models derived from just three sets of patient level data.
- The patient level data on which the regression models were based contained predominantly patients receiving CPAP. To ameliorate this problem, future trials would ideally incorporate generic instruments to provide a direct measure of preference-based health-related quality of life (HRQoL).

Uncertainties

- The effectiveness (and hence cost-effectiveness) of using CPAP to treat mild disease remains uncertain due to a paucity of research; the treatment effect for daytime sleepiness in the current review is based on only two studies.
- The relative treatment benefits with CPAP according to symptom severity are based on summary data and cannot be viewed as definitive.
- The patients studied in most trials tend to be middle aged and predominantly male. It is unclear whether therapeutic benefits are similar in other groups, in particular the elderly where cognitive impairment and cerebrovascular disease are more prevalent and the obstructive sleep apnoea/hypopnoea syndrome (OSAHS) may be complicated.
- Dental devices may be a treatment option in moderate disease. However, there was inconsistency in the treatment effect comparing CPAP and dental devices, possibly due to the variety of dental devices investigated. It remains unclear precisely what type of devices may be effective and in which populations with OSAHS. The effectiveness of dental devices compared to CPAP in mild and severe disease populations is unclear.

Refer to Sections 8.2, 8.3, and 8.4 of the Assessment Report (see the "Availability of Companion Documents" field) for additional information on limitations and uncertainties of the Assessment.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by

Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (www.nice.org.uk/TA139; see also the "Availability of Companion Documents" field).
    - Slides highlighting key messages for local discussion.
    - Local costing template incorporating a costing report to estimate the savings and costs associated with implementation.
    - Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
    - Audit support for monitoring local practice.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 25 p. (Technology appraisal guidance; no. 139).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Mar

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 2 p. (Technology appraisal 139). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. Costing template and report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. Various p. (Technology appraisal 1139). Available in Portable Document Format (PDF) from the NICE Web site.
- Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 7 p. (Technology appraisal 139). Available in Portable Document Format (PDF) from the NICE Web site.
- Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome: implementing NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 15 p. (Technology appraisal 139). Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1493. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Continuous positive airway pressure for obstructive sleep apnoea/hypopnoea syndrome. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 4 p. (Technology appraisal 139). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1494. 11 Strand, London, WC2N 5HR.

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